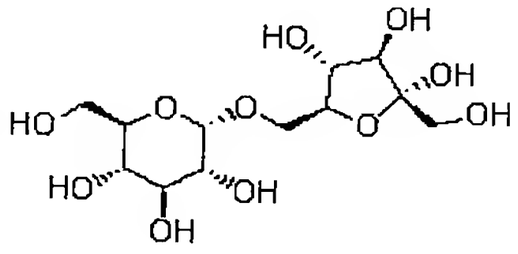
Palatinose

Identification

Name	Palatinose
Synonyms	6-O-alpha-D-Glucopyranosyl-D-fructofuranose; Isomaltulose
Molecular Structure	
Molecular Formula	$C_{12}H_{22}O_{11}$
Molecular Weight	342.30
CAS Registry Number	58166-27-1
EINECS	261-150-2

Properties

Melting point	125-128 °C
alpha	100 ° (c=2, H2O)

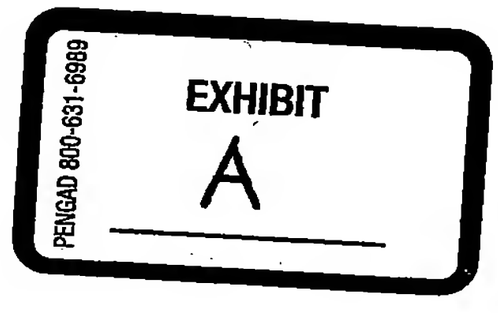
Safety Data

Safety Description	S24/25 Details

List of Suppliers

The Complete List of Suppliers for Palatinose

U.S. Patent Application 10/715,125

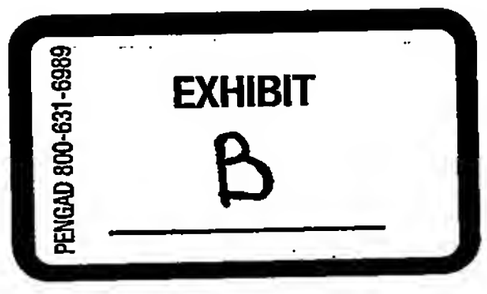


Pachymic acid Paclitaxel Paclobutrazol Padimate Paeoniflorin Paeonol Paliperidone Palladium Palladium(II) acetylacetonate Palladium bromide Palladium chloride Palladium diacetate Palladium hydroxide Palladium monoxide Palladium nitrate Palladium sulfate Palmatine Palmatine chloride Palmatine chloride hydrate Palmitic acid Palmitic anhydride N-Palmitoyl-L-serine Palonosetron Palonosetron Palonosetron hydrochloride Pamabrom Pamidronate disodium salt Pamidronic acid Panaxadiol Panaxatriol Pancreatin Pancuronium bromide Panipenem Panthenol DL-Pantolactone Pantoprazole Pantoprazole sodium Pantothenyl ethyl ether DL-Pantothenyl ethyl ether Papain Papaverine hydrochloride [2.2]Paracyclophane Paraffin wax Paraformaldehyde Paraldehyde Paramethasone Paraquat Paraquat dichloride Paraquat methosulfate

Online Edition: "Combined Compendium of Food Additive Specifications"

Additive	**Isomalt**
Synonym(s)	Hydrogenated isomaltulose
Specification	Monograph 1 (2006) Monograph 5 (2008)
Codex specification	INS number: 953

U.S. Patent Application 10/715,125



ISOMALT

Prepared at the 46th JECFA (1996), published in FNP 52 Add 4 (1996) superseding specifications prepared at the 39th JECFA (1992), published in FNP 52 Add 1 (1992). Metals and arsenic specifications revised at the 57th JECFA (2001). An ADI 'not specified' was established at the 29th JECFA (1985)

SYNONYMS Hydrogenated isomaltulose; INS No. 953

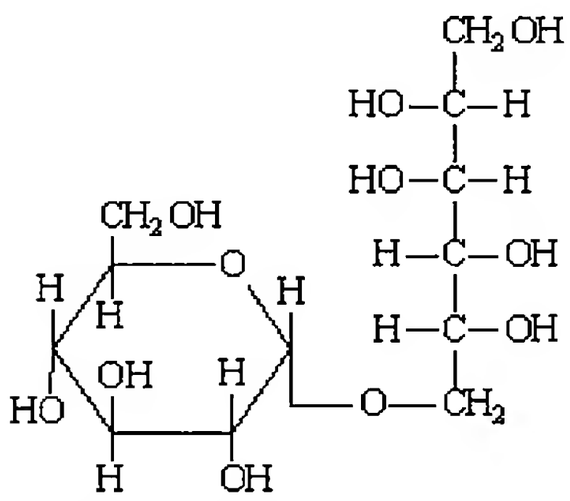
DEFINITION A mixture of hydrogenated mono- and disaccharides whose principal components are the disaccharides:

Chemical names
6-O-alpha-D-Glucopyranosyl-D-sorbitol (1,6-GPS) and
1-O-alpha-D-Glucopyranosyl-D-mannitol dihydrate (1,1-GPM)

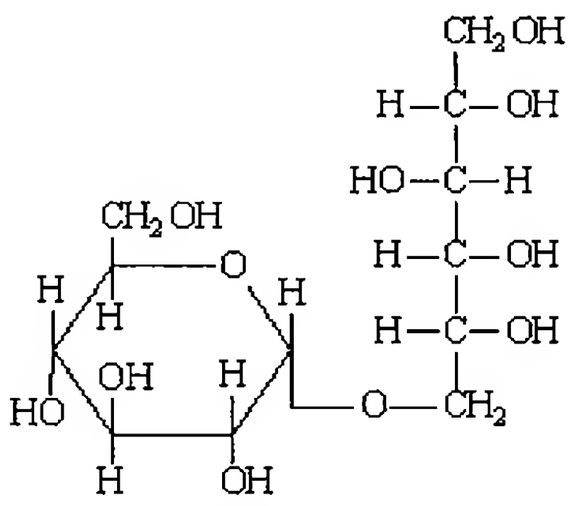
C.A.S. number 64519-82-0

Chemical formula
6-O-alpha-D-Glucopyranosyl-D-sorbitol: $C_{12}H_{24}O_{11}$
1-O-alpha-D-Glucopyranosyl-D-mannitol dihydrate: $C_{12}H_{24}O_{11} \cdot 2H_2O$

Structural formula



6-O-alpha-D-Glucopyranosyl-D-sorbitol



1-O-alpha-D-Glucopyranosyl-D-mannitol (without molecules of crystal water)

Formula weight
6-O-alpha-D-Glucopyranosyl-D-sorbitol: 344.32
1-O-alpha-D-Glucopyranosyl-D-mannitol dihydrate: 380.32

Assay Not less than 98% of hydrogenated mono- and disaccharides and not less than 86% of the mixture of 6-O-alpha-D-glucopyranosyl-D-sorbitol

and 1-O-alpha-D-glucopyranosyl-D-mannitol on the anhydrous basis

DESCRIPTION Odourless, white, crystalline slightly hygroscopic substance

FUNCTIONAL USES Sweetener, bulking agent, anticaking agent, glazing agent

CHARACTERISTICS

IDENTIFICATION

Solubility (Vol. 4)	Soluble in water, very slightly soluble in ethanol
Thin layer chromatography (Vol. 4)	Passes test See description under TESTS

PURITY

Water (Vol. 4)	Not more than 7.0% (Karl Fischer Method)
Sulfated ash (Vol. 4)	Not more than 0.05% Test 5 g of the sample (Method I)
D-Mannitol	Not more than 3% See Method of Assay
D-Sorbitol	Not more than 6% See Method of Assay
Reducing sugars (Vol. 4)	Not more than 0.3% Proceed as directed under *Reducing Substances (as glucose)*, Method II. The weight of cuprous oxide shall not exceed 50 mg.
Nickel (Vol. 4)	Not more than 2 mg/kg See description under TESTS
Lead (Vol. 4)	Not more than 1 mg/kg Prepare a sample solution as directed in the Limit Test for organic compounds and determine the lead content by *atomic absorption spectrometry*

TESTS

IDENTIFICATION TESTS

Thin layer chromatography	TLC plates TLC aluminium foils or plates of approx. 12 cm length and coated with a layer of approx. 0.2 mm, Kieselgel 60 F_{254}, Art. 5554, Merck, or equivalent Reference solution Dissolve 500 mg of each of the following sugar alcohols in 100 ml of water: Sorbitol, mannitol, lactitol, maltitol, 1-O-alpha-D-gluco-pyranosyl-D-mannitol (1,1-GPM), and 6-O-alpha-D-glucopyranosyl-D-sorbitol (1,6-GPS)

U.S. Patent Application 10/715,125

Food Sci. Technol. Res., **13** (1), 81–84, 2007

Note

Addition Ratio of Palatinose and Body Fat Accumulation in Mice

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In the present study, the relationship between the addition ratio of palatinose in feed and body fat accumulation was investigated in mice. Thirty eight-week-old male mice (C57BL/6CrSlc) were divided into three groups: a 0% palatinose group (control group), a 18% palatinose group, and an 40% palatinose group. The 3 groups were then fed their respective diets for 8 weeks. Following the conclusion of the feeding period, fat tissues in the perirenal, periepididymal, and perimesenteric regions were removed to determine their wet weight. The weight of the visceral fat was clearly lower in mice of groups fed with feed containing palatinose than in the mice of the control group. In particular, the weight of perirenal fat was significantly lower in the 40% palatinose group than in the control group ($p < 0.05$).

Keywords: blood glucose, insulin, enzyme inhibition, internal organ fat, lipo-protein lipase

Introduction

Palatinose (6-O-D-glucopyranosyl-D-fructofuranose), also known as isomaltulose, has been used in a variety of food products as a noncariogenic (Ooshima *et al.*, 1983) natural sugar with sucrose-like superior taste (Kaga and Mizutani, 1985). The calorie count of palatinose is 4 kcal/g; the same as that of sucrose. Palatinose is characterized by its slow rate of digestion and absorption. It is digested at a rate approximately 1/5 that of sucrose (Tsuji *et al.*, 1986), resulting in only gradual increases in blood glucose levels (Kawai *et al.*, 1985, 1989). The glycemic index (GI) of palatinose is estimated to be 44. Despite the slow rate of digestion, there are numerous enzymes in the small intestine that are able to digest palatinose, and ingestion of a large amount of the sugar does not cause diarrhea. Thus, palatinose is a safe sugar to consume. Recently, several reports have been published on the functions of palatinose associated with gradual increases in blood glucose levels (Kashimura *et al.*, 2003; Nagai *et al.*, 2003).

Meanwhile, GI has recently been drawing worldwide attention with relation to health (Jenkins *et al.*, 2002; Willet *et al.*, 2002), particularly with that of obesity (Brand-Miller *et al.*, 2002). A mechanism is postulated whereby increased blood glucose level leads to an increase in insulin level and lipoprotein lipase (LPL) activity in fat tissues, resulting in lipid uptake in fat tissues (Suzuki, 1987).

In a study in which palatinose was fed to rats in place of sucrose, it was reported that accumulation of visceral fat was suppressed compared with animals fed with sucrose, and that there was little increase in LPL activity in fat tissues of rats fed with feed containing palatinose (Mizutani, 1989). In recent years, we have discovered that palatinose suppresses the increase in blood glucose level caused by sucrose or glucose ingestion (Kashimura *et al.*, 2003). These results suggest the possibility that palatinose may suppress blood glucose increase, thereby suppressing obesity and accumulation of visceral fat associated with lifestyle-related diseases. Here we investigate the relationship between the addition ratio of palatinose in feed and fat accumulation in mice.

Materials and Methods

Animals Thirty seven-week-old male mice (C57BL/6 CrSlc) were acclimatized for one week and fed commercial powder feed (CRF-1, Oriental Yeast) and given water in a room maintained at 22±3°C and 50±20% relative humidity with ventilation 13 to 17 times/hour and illumination from 8:00 to 20:00 (12-hour light and dark cycles). After acclimatization, the mice were divided into 3 groups of 10 (0% palatinose group [control group], 18% palatinose group, and 40% palatinose group) by stratified continuous randomization method using body weight as the index, and then housed individually in polycarbonate cages. At group assignment, it was confirmed that there was no significant difference in body weight among groups. Mice in each group were subjected to pair feeding using the feed shown in Table 1, with tap water ad libitum, for 8 weeks.

Test parameters: Feed consumption was measured everyday, during the feeding period, and body weight was measured every week. The animals had been fed with feed and tap water until the amount of intake of feed was measured on the day when the anatomy was to be performed. Following that, the abdominal cavity of the mice was opened under a subnarcotic condition with ether and 1 ml of blood was collected from the postcava, and subsequently left to exsanguinate. Subsequently,

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Table 1. Composition of Experimental Diets.

Component/group	0% palatinose (control group)	18% palatinose	40% palatinose
Corn starch	14.95	14.95	14.95
Sucrose	40.00	22.00	0.00
Palatinose	0.00	18.00	40.00
Cellulose	5.00	5.00	5.00
Soybean oil	15.00	15.00	15.00
Mineral mixture(AIN93G)	3.50	3.50	3.50
Vitamin mixture(AIN93G)	1.00	1.00	1.00
L-cystine	0.30	0.30	0.30
Choline hydrogen tartrate	0.25	0.25	0.25
Casein	20.00	20.00	20.00

Table 2. Body Weight Gain.

	Intial weights	Final wieghts
0% palatinose group (control group)	24.0±0.3	36.2±0.8
18% palatinose group	23.7±0.3	32.8±0.9*
40% palatinose group	23.8±0.3	33.5±0.8*

Data were expressed as Mean (g)±SD

*Statistically significant at the $p<0.05$ level when compared with the data obtained in the control group.

Table 3. Effects of Palatinose Administration on Body Fat Accumulation in Male Mice.

	0% palatinose group (control group)	18% palatinose group	40% paltinose group
Fat tissue in the perirenal region	1.98±0.22	1.73±0.43	1.61±0.46*
Fat tissue in the periepididymal region	3.91±0.72	3.58±0.65	3.48±0.64
Fat tissue in the perimesenteric region	1.46±0.28	1.46±0.43	1.40±0.47

Data were expressed as Mean (wet g/100g B.W.)±SD

*Statistically significant at the $p<0.05$ level when compared with the data obtained in the control group.

fat tissues (perirenal, periepididymal, and perimesenteric regions) were removed and measured for wet weight. Collected blood was centrifuged to obtain serum, which was measured for free fatty acids, triglycerides, phospholipids, and total cholesterol using a Hitachi 7070 automatic analyzer.

Statistical method: Data obtained were subjected to testing for homogeneity of variance and, if found to be homogenous, subjected to unpaired t-test. Significance levels were set at 5% and 1%, respectively.

This study was done in accordance with the guidelines of the Japanese Association for Laboratory Animal Science, 1987.

Results

General conditions: Throughout the study period, none of the animals in any group exhibited evidence of diarrhea or loose stools, symptoms often observed when non- or low- digestible sugars are ingested. No other abnormalities in general conditions were observed either.

Feed consumption: No difference was observed in feed consumption among groups throughout the feeding period.

Body weight: Changes over time of body weight in each group during the feeding period are shown in Table 2. Body weight gain was slightly slower in the 18% palatinose and 40% palatinose groups when compared with the control group. As a result, significantly lower body weight in both palatinose and control groups were observed at the end of the feeding period ($p<0.05$).

Fat tissue weight: Table 3 shows the weight per 100 grams of body weight for fat tissues in the perirenal, periepididymal, and perimesenteric regions of animals in each group. It was observed that there was a general tendency of the weight of the visceral fat becoming lower in the mice of the groups fed with feed containing palatinose.

In particular, the weight of perirenal fat was significantly lower in the 40% palatinose group when compared with that of the control group ($p<0.05$). The weight of the visceral fat in the 40% palatinose group was lower than the weight in the 18% palatinose group, however the difference was insignificant.

Blood biochemistry: Changes over time of blood bio-

Table 4. Effect of Palatinose Administration on Blood Chemistry in Male Mice.

	0% palatinose group (control group)	18%palatinose group	40%palatinose group
Triglyceride (mg/dL)	18±2	21±2	24±2*
Phospholipid (mg/dL)	249±14	229±6	244±6
Total cholesterol (mg/dL)	144±10	130±5	143±4
NEFA(μEq/L)	410±37	460±50	397±26

Data were expressed as Mean±SE

*Statistically significant at the $p<0.05$ level when compared with the data obtained in the control group.

chemistry are shown in Table 4. Triglycerides showed a tendency to increase with palatinose consumption, being significantly higher in the 40% palatinose group than in the control group ($p<0.05$). No marked difference was observed in free fatty acids, phospholipids or total cholesterol level among groups.

Discussion

In this study, the body weight of animals in the 18% and 40% palatinose groups was significantly lower than the body weight of animals in the control group despite the fact that there was no difference in feed consumption among the groups throughout the study period. A possible cause of this result is water of crystallization contained in the palatinose. Since palatinose contains approximately 5% water as crystallization water, the net amount of palatinose is 5% less than that of sucrose. However, in terms of the entire amount of feed, this difference is only 2% for the 40% palatinose group and 0.9% for the 18% palatinose group, whereas a difference of approximately 10% was observed in body weight between the palatinose groups and the control group at the end of the feeding period. This suggests that the difference was not due to the water content of palatinose but to changes induced by the difference in digestibility and absorption between the two types of sugars.

It was reported that when palatinose was consumed together with sucrose or glucose, the increase in blood glucose level was smaller than that observed when sucrose or glucose was consumed alone (Kashimura *et al.*, 2003). This blood glucose-suppressing effect of palatinose is postulated to be caused by inhibition of enzymes such as sucrase, maltase and glucoamylase (Kashimura *et al.*, 2005). The fact that blood glucose increase induced by glucose is also suppressed suggests that palatinose inhibits, not only the activity of the above enzyme, but also the absorption of glucose. From these results, it is thought that palatinose, when consumed together with sucrose or starch, may suppress the increase in blood glucose level induced by sucrose or starch. In fact, 18% palatinose was as equally effective as 40% palatinose in suppressing fat accumulation. This is because palatinose is active in suppressing the increase in blood glucose induced by sucrose or glucose in addition to its function as a low glycemic substance. It is postulated that the reason why blood triglyceride levels were higher in the palatinose groups than in the control group is because, in the present study, animals were fed with feed until the day an anatomy was performed, thereby bringing about high triglyceride values. There was a report concerning SD rats where blood triglyceride levels were found rather lower in a group of animals fed with a fluid diet containing palatinose as the main ingredient for 2 months than in a group fed with commercially available solid feed (Arai *et al.*, 2003).

With regard to the effective addition ratio of palatinose in suppressing fat accumulation, the ratio of 10% or more, relative to sucrose or starch, has been found to be effective in inhibiting enzyme activities (Kashimura *et al.*, 2005). In the present study, the percentage of palatinose to total carbohydrate was approximately 32% in the 18% palatinose feed group. Since fat accumulation is directly regulated by insulin, and blood glucose level should therefore change to an extent sufficient to induce insulin secretion, the required addition ratio of palatinose may be higher than that sufficient for inducing enzyme inhibition.

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United States Patent [19]

Coia et al.

[11] **Patent Number: 4,971,798**

[45] **Date of Patent: Nov. 20, 1990**

[54] **HARD CONFECTIONS CONTAINING HYDROGENATED ISOMALTULOSE AND MEDICINALLY ACTIVE INGREDIENT**

[75] Inventors: **Kenneth A. Coia**, Elkhart, Ind.; **Michael J. Lynch**, Bridgewater, N.J.

[73] Assignee: **Miles Inc.**, Elkhart, Ind.

[21] Appl. No.: **443,182**

[22] Filed: **Nov. 30, 1989**

[51] **Int. Cl.**[5] **A61K 9/20**; A61K 9/22

[52] **U.S. Cl.** **424/440**; 514/777; 514/849; 514/850; 514/853; 514/948

[58] **Field of Search** 424/440

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Primary Examiner—Shep K. Rose

Attorney, Agent, or Firm—Jerome L. Jeffers

[57] **ABSTRACT**

Disclosed is a hard confection containing Palatinit (hydrogenated isomaltulose) and a medicinally active ingredient. Such a formulation has been found to dissolve more slowly than similar formulations based on sugar rendering them suitable for dispensing the active ingredient over an extended period of time.

10 Claims, No Drawings

U.S. Patent Application 10/715,125

HARD CONFECTIONS CONTAINING HYDROGENATED ISOMALTULOSE AND MEDICINALLY ACTIVE INGREDIENT

BACKGROUND OF THE INVENTION

Hydrogenated isomaltulose sold under the tradename Palatinit ® by the Palatinit GmbH of Mannheim, Germany, also known as isomalt, is a sugar substitute which can be used in place of sucrose, glucose or similar sugars for the production of foodstuffs. This material may be classified as a carbohydrate, more specifically, as a hydrogenated disaccharide. The production of hydrogenated isomaltulose involves an enzymatic rearrangement of saccharose into a more stable compound known as isomaltulose (tradename Palatinose). Following a purifying crystallization, the isomaltulose is hydrogenated to form the resulting Palatinit which is described as an odorless, white, crystalline, nonhygroscopic substance containing about 5 percent water of crystallization. This material contains approximately 2.1 calories/gm and has a sweetness of about half that of sucrose. The reduced caloric value results from the fact that Palatinit is only partially metabolized, so that its caloric utilization is only 2.1 calorie per gram.

In U.S. Pat. No. 4,792,453 there is disclosed a hard coated chewing gum comprising a sugarless chewing gum center having a hard coating comprising hydrogenated isomaltulose preferably in an amount of from 50 to 75 weight percent of the coating.

There is disclosed in U.S. Pat. No. 4,840,797 a confectionary or pharmaceutical product having a hard, sugarless coating, comprising xylitol, mannitol or maltitol. Sorbitol is also mentioned in this regard.

Published European Patent Application 0 303 295 A_2 describes a hard candy comprising meso-erythritol as the main component together with other saccharides such as sucrose, glucose, thick malt syrup, fructose, and isomerized sugars as well as palatinose and isomaltose.

U.S. Pat. No. 4,587,119 discloses the use of isomaltulose as a total or partial substitute for sucrose in the preparation of food and pharmaceutical products for human or animal consumption. This patent mentions orally-administered ingested pharmaceutical compositions as well as those which are taken into the mouth but not with the intent of being ingested such as toothpastes, tooth powders, mouth washes, gargles, dental lotions and chewing gums.

SUMMARY OF THE INVENTION

The present invention is a hydrogenated isomaltulose based hard confection which contains, in addition to the hydrogenated isomaltulose, a medicinally active ingredient.

DESCRIPTION OF THE INVENTION

The term hard confections refers to amorphous products prepared by evaporation of water from a sugar solution so as to concentrate it to a solid content of not less than 95% by weight. The present invention involves replacing the sugar with Palatinit, i.e. hydrogenated isomaltulose, and incorporating therein an active ingredient to produce solid confections containing one or more active, medicinal ingredient.

Presently, the preferred method of manufacturing hard confections involves cooking sugar solutions in a kettle under constant slow agitation until the solution starts to boil. Agitation is discontinued and the pressure

is dropped to 22–25 inches of Hg whereupon the mix is held under this slight vacuum for a period of from 3–10 minutes. Typically, the sugar mix is heated to 266°–320° F., preferably 280°–310° F. Acids, color and/or flavorings are added and the mix is either molded or stamped into various shapes and sizes. As compared to what might be expected based on the manufacture of sugar hard confections, Palatinit containing hard confections require higher temperatures of 300–330° F. for manufacturing. Palatinit is suitable for use in hard confections because of its sweet taste and contributes low caloric content. The discovery that Palatinit based confections dissolve more slowly than those containing sugar renders this material particularly suitable for use in a hard confection containing an active, medicinal ingredient due to the longer duration of medicinal activity that can be achieved thereby.

Typically, medicinal agents that can be added to the Palatinit based hard confection are antitussives, e.g. dextromethorphan hydrobromide as well as decongestants, antihistamines and/or expectorants.

More particularly, if it is desired to treat a sore throat, cough and nasal congestion one could combine hexylresorcinol (2.4 mg) and menthol (10 mg) in a unit dosage form of the hard confection. When nasal congestion is the problem, phenylpropanolamine hydrochloride (25 mg) may be added or in the case of a mild sore throat hexylresorcinol (2.4 mg) or dyclonine hydrochloride would be indicated. When suppression of a cough combined with a sore throat is indicated one could use a combination of dextromethorphan hydrobromide (5.0 mg), menthol (5.0 mg), menthol eucalyptus (5.0 mg), benzocaine (5.0 mg) and cetylpyridinium (1.66 mg) where menthol and eucalyptus serve the dual function of medicament and flavoring agent.

A typical formulation will contain, on a w/w basis, 50 to 98% Palatinit and from 1.0 to 15 mg per dosage of the active ingredient. The confection will normally contain other ingredients such as flavoring agents; e.g. oils derived from plants and fruits such as citrus oils and fruit essences; artificial sweeteners to enhance the sweetening power of Palatinit; e.g. Aspartame, Acesulfame-K, and saccharin, flavoring agents; e.g. natural or synthetic flavors and/or oils derived from plants, leaves, flowers and fruits such as lemon, honey, cherry, menthol, eucalyptus, peppermint and spearmint; natural or synthetic coloring agents and perhaps a binding agent selected from the group of alginate, cellulosic, vegetable gums and the like.

Flavoring agents contemplated for use in the present invention may be added to the hot syrup in an amount such that the finished confection will contain from about 0.05 to 0.3 weight percent and preferably 0.1 to 0.2 weight percent of the flavoring material. Artificial sweeteners, when used, are typically added to the syrup in sufficient amount to provide the desired sweetness in the finished products. The amounts used will depend on the sweetening power of the particular artificial sweetener selected and will typically range from 0.05 to 0.25 weight percent of the finished formulation. Coloring agents are typically food quality dyes or lake added directly to the syrup in the dye form. Exemplary of such dyes are Blue #1 or #2, Red #3 plus #40, Yellow #5 or #6, titanium dioxide or blends of these dyes selected to produce the desired color. Alternatively, natural colors such as carmine, annatto, beta carotene, turmeric, beet, grape skin extract, caramel, and blends thereof may be

used as the colorant. Typical use levels for the coloring agent range from 0.01 to 0.03% for synthetic dyes with levels of from 0.1 to 1.0% for the natural colorants. In addition, organic acids are typically added to the formulation for the purpose of providing tartness. Suitable acids include citric, malic, maleic, fumaric, succinic, adipic and tartaric acid.

A typical formulation will contain:

Ingredient	Wt %	Preferred %
Palatinit	10.0–99.0	50–98
Acid	0.1–5.0	0.2–2.5
Flavor	0.01–2.5	0.05–0.3
Color	0.01–2.0	0.05–1.5
Sweetener	0.05–0.3	0.05–0.25
Active Ingr.	0.05 mg–25 mg	1.0 mg–15.0 mg

which ingredients have been formulated in the manner described above. The method of practicing the present invention, and the slower dissolution rate achieved by replacing sugar with Palatinit in the hard confection, are illustrated by the following examples.

EXAMPLE I

The purpose of the experiment described in this example was to determine whether the use of Palatinit as a functional replacement for sugar and corn syrup in hard confections results in a longer dissolution time. The active ingredients used in this study were:

Sucrose (commercial grade)
Palatinit (type N coarse material for hard candies)
Corn Syrup (42DE from ADM Sweeteners)
Sunnette (Acesulfame-K from Hoechst Celanese Corp.)
FD&C Red #40 (Warner-Jenkinson Co.)
Artificial Cherry Flavor (H-5345 from Haarmann & Reimer Corp.)

Hard candies (with sugar/corn syrup or Palatinit having the following formulations were prepared:

Ingredients	%
SUGAR HARD CANDY FORMULATION	
Sucrose	49.360
42DE Corn Syrup	32.910
Water	16.622/15.642
Citric Acid/Buffered Citric Acid*	0.800/1.780
FD & C Red #40 (5% Sol)	0.078
Artificial Cherry Fl. (H-5345)	0.120
Sunnette (Acesulfame-K)	0.110
	100.000
PALATINIT HARD CANDY FORMULATION	
Palatinit (type N)	74.900
Water	23.992/23.012
Citric Acid/Buffered Citric Acid*	0.800/1.780
FD & C Red #40 (5% Sol)	0.078
Artificial Cherry Fl. (H-5345)	0.120
Sunnette (Acesulfame-K)	0.110
	100.000

*45% Citric acid
15% sodium citrate
40% water

PREPARATION

The sugar candies were prepared by adding the 42DE corn syrup to a stainless steel pan followed by the addition of water. This mixture was heated and mixed to dissolve the corn syrup in water whereupon the sucrose was added with heating up to 300° F. The sugar mixture was cooled to 290° F. and citric acid (buffered or unbuffered) was added followed by the addition of Sunnette, color and flavor. The 60% buffered citric acid solution was prepared by heating 150 g citric acid, 50 g sodium citrate, and 133.3 g D.I. water. This formulation was molded at either 280° F. or 260° F. to form hard candies.

The Palatinit containing candies were prepared by adding water to the stainless steel pan along with Palatinit (type N). The mixture was heated to dissolve the Palatinit and then boiled at temperatures to 320° F. The Palatinit containing mixture was cooled to 290° F. and citric acid (buffered or unbuffered) was added, followed by the addition of Sunnette, color and flavor and molded at either 280° F. or 260° F. into the form of hard candies.

All candies were placed into glass jars with lids tightly secured. The candies were held for 24 hours or 48 hours before dissolution tests were conducted.

DISSOLUTION TEST

A disintegration tester was used to determine the dissolution rate of the candies prepared as described above. After weighing, the candies were placed into the tubes of the tester's basket which was placed into a 1 liter beaker with 800 ml of buffered saline solution at 37.5° C. The buffered saline solution contained 308 ml of 0.1 M citric acid, 692 ml 0.2 M dibasic sodium phosphate, 1.17 g NaCl and approximately 1 liter D.I. water to provide a 2 liter quantity. The pH of the buffered saline solution was approximately 6.7 to simulate the pH of saliva; the NaCl was used to simulate its salinity.

The candies used for the dissolution test weighed approximately 3.5 g each. There were 3 determinations consisting of a total of 18 replications which were averaged out to give the mean dissolution time in minutes.

RESULTS AND DISCUSSION

A factorial experiment was designed in which analysis of 16 runs were used to estimate the effects of acid type (citric acid or buffered citric acid), molding temperature (260 or 280° F.), and age prior to measurement time on the dissolution rate of the hard candies being tested which contained either sugar/corn syrup or Palatinit. In the design of this experiment, a particular treatment (independent variable) is referred to as a factor. This factorial experiment had four key factors affecting dissolution rate. They are:

(a) dissolution measurement time (24 and 48 hours).
(b) molding temperature 260 and 280° F.),
(c) acid type (citric acid and buffered citric acid), and
(d) sucrose or Palatinit.

Table 1 shows the factorial design and the results of the dissolution times (minutes) for each run; Table 2 shows the effects and interactions.

TABLE I

Run	A Hr	B F.	C Acid	D	Dissolution Time (Min)
1	24	260	citric	sugar	14.260
2	48	260	citric	sugar	14.140
3	24	280	citric	sugar	14.570
4	48	280	citric	sugar	14.950
5	24	260	BCA	sugar	14.320
6	48	260	BCA	sugar	14.020
7	24	280	BCA	sugar	14.710
8	48	280	BCA	sugar	14.840
9	24	260	citric	PAL	14.470
10	48	260	citric	PAL	15.950
11	24	280	citric	PAL	15.780
12	48	280	citric	PAL	15.780

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 4,971,798
DATED : November 20, 1990
INVENTOR(S) : COIA et al.

It is certified that error appears in the above-indentified patent and that said Letters Patent is hereby corrected as shown below:

Claim 1, line 5: before "isomaltulose" insert
--hydrogenated--.

Signed and Sealed this
Seventeenth Day of June, 1997

Attest:

Attesting Officer

BRUCE LEHMAN
Commissioner of Patents and Trademarks

U.S. Patent Applicn 10/715,125

ABOUT GLYCEMIC INDEX

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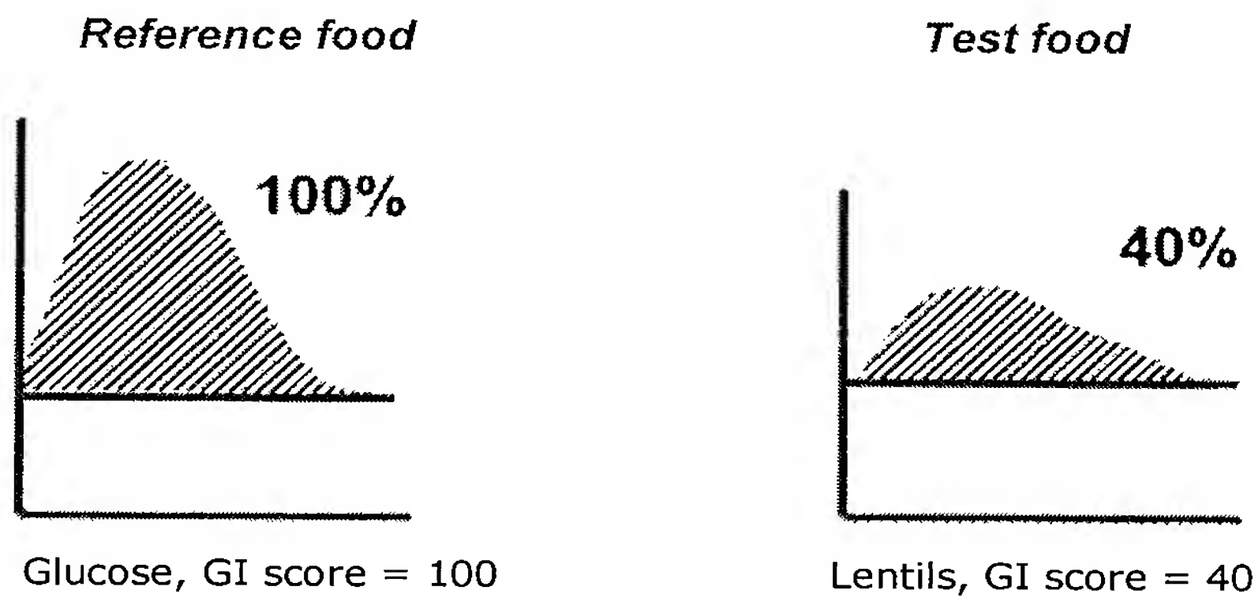
The glycemic index (GI) is a ranking of carbohydrates on a scale from 0 to 100 according to the extent to which they raise blood sugar levels after eating. Foods with a high GI are those which are rapidly digested and absorbed and result in marked fluctuations in blood sugar levels. Low-GI foods, by virtue of their slow digestion and absorption, produce gradual rises in blood sugar and insulin levels, and have proven benefits for health. Low GI diets have been shown to improve both glucose and lipid levels in people with diabetes (type 1 and type 2). They have benefits for weight control because they help control appetite and delay hunger. Low GI diets also reduce insulin levels and insulin resistance.

Recent studies from Harvard School of Public Health indicate that the risks of diseases such as type 2 diabetes and coronary heart disease are strongly related to the GI of the overall diet. In 1999, the World Health Organisation (WHO) and Food and Agriculture Organisation (FAO) recommended that people in industrialised countries base their diets on low-GI foods in order to prevent the most common diseases of affluence, such as coronary heart disease, diabetes and obesity.

Measuring the GI

To determine a food's GI rating, measured portions of the food containing 10 - 50 grams of carbohydrate are fed to 10 healthy people after an overnight fast. Finger-prick blood samples are taken at 15-30 minute intervals over the next two hours. These blood samples are used to construct a blood sugar response curve for the two hour period. The area under the curve (AUC) is calculated to reflect the total rise in blood glucose levels after eating the test food. The GI rating (%) is calculated by dividing the AUC for the test food by the AUC for the reference food (same amount of glucose) and multiplying by 100 (see Figure 1). The use of a standard food is essential for reducing the confounding influence of differences in the physical characteristics of the subjects. The average of the GI ratings from all ten subjects is published as the GI of that food.

Figure 1. ***The two hour blood sugar response of a high-GI food vs a low-GI food***



> The amount of carbohydrate (startch & sugars) in the reference and test foods must be the same.

The GI of foods has important implications for the food industry. Some foods on the Australian market already show their GI rating on the nutrition information panel.Terms such as complex carbohydrates and sugars, which commonly appear on food labels, are now recognised as having little nutritional or physiological significance. The WHO/FAO recommend that these terms be removed and replaced with the total carbohydrate content of the food and its GI value. However, the GI rating of a food must be tested physiologically and only a few centres around the world currently provide a legitimate testing service. The Human Nutrition Unit at the University of Sydney has been at the forefront of glycemic index research for over two decades and has tested hundreds of foods as an integral part of its program. Jennie Brand Miller (JBM) is the senior author of International Tables of Glycemic Index published by the American Journal of Clinical Nutrition in 1995 and 2002.

Glycemic Index Books

Jennie Brand-Miller's books, The New Glucose Revolution, The New Glucose Revolution LifePlan and related pocket books on diabetes, heart disease and weight reduction are aimed at lay people and health professionals, and have sold more than 1.7 million copies around the world since 1996. The UK edition was released in 1997 and the North American edition (The Glucose Revolution) in July 1999. There are Dutch, French, Danish, Swedish, Norwegian, Spanish, Polish and Japanese editions also on the market. All versions include back-of-book tables of the GI values of some 600 different foods, many of them tested in the Human Nutrition Unit. Popular health books and articles in women's magazines by other authors on topics as diverse as breast cancer and weight loss have also included GI tables. These publications have generated an increasing demand for GI testing.

Glycemic Index Symbol Program

The GI Symbol Program [http://www.gisymbol.com.au] was launched in Australia in 2002 to help consumers identify the GI of foods. Foods that carry the symbol are guaranteed to have been properly tested by an accredited laboratory.

In the near future, many more foods are likely to carry the GI on their nutrition panel. The services of a professional GI testing service such as SUGiRS will therefore allow food companies to take advantage of GI marketing opportunities.